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## TITLE OF INVENTION

### METHOD FOR PLASMA CHARGING A PROBE

#### Claim of Priority

This application derives priority from co-pending U.S. Serial No. 60/176,201 filed January 14, 2000, and is a continuation-in-part of U.S. Serial No. 09/765,733 filed January 12, 2001 and PCT US01/01262 filed January 12, 2001.

#### Field of the Invention

The present invention relates to a method for use of plasma to apply a controlled charge to a surface.

#### Background of the Invention

Within the disciplines of the clinical, industrial and life science laboratory, scientists perform methods and protocols with extremely small quantities of fluids. These fluids consist of many categories and types with various physical properties. Many times volumes are worked with that are between a drop (about 25 microliters) and a few nanoliters. There are a number of standard methods employed to transfer liquid compounds from a source by aspirating the liquid from such fluid holding device into the fluid dispensing device having a probe, cannula, pin tool or other similar component or plurality of components which move, manually or robotically, and then dispensing, from the same probe or plurality of probes, into another fluid holding device.

Four common techniques are (1) a scheme using a probe or cannula, that may or may not be coated with a layer of material or special coating, which is attached directly or by a tube to a pumping device, (2) a scheme using a disposable pipet instead of the probe/cannula but otherwise similar, (3) a scheme using a spray head with one or a plurality of openings and pumping system that physically propels multiple precisely metered microdroplets, and (4) a scheme using metal shafts with precisely machined hollowed out spaces at their ends that hold the fluid by surface tension (commonly referred to as a "pin tool").

As routine a process as fluid transfer is in the laboratory, technical challenges to achieve suitable levels of precision and accuracy remain. As the volume decreases, it becomes progressively more technically challenging to aspirate and dispense these very small quantities of fluids due to the various effects of interaction between the dispensing device and the fluid. Droplet formation, as the fluid is dispensed, is a change in the shape of the fluid. The droplet experiences changes in internal forces during the process (e.g., surface tension, viscosity, and polarity) and in external forces due to interactions between the fluid and the surfaces of the probe, cannula, pin tool or other similar component (e.g., superficial and interfacial energies). It is desirable to control and be able to use these forces to improve the process. The use of low temperature atmospheric plasma in such a way so as to place a charge on the probe, cannula, pin tool or other similar component, in order to control properties of the surface of the probe, cannula, pin tool or other similar component in order to attract or repel the fluid accomplishes this desired objective. This control is

achieved by metering the deposition of charge by the plasma. The optimum conditions for fluid transfer can be reached taking into consideration the application, fluid characteristics, the affect of any compound dissolved in the liquid, the affect of any particles or other physical matter in the liquid and the type of probe or delivery mechanism used.

The charge from the plasma on the surfaces of the probe, cannula, pin tool or other similar component will alter forces effecting droplet formation, the force required to release the droplet from the probe, cannula, pin tool or other similar component, the surface tension interaction between the liquid and the probe, cannula, pin tool or other similar component, and help suppress the formation of microdroplets (parts of the fluid being transferred that can break off) during dispensing. Some fluid dispensing devices allow the plasma to be pulled into the internal spaces of the probe, cannula or other similar component. The plasma generated surface effects on the fluid inside will have similar action as on the outside surfaces. Exposing the internal surfaces of the probe, cannula or other similar component adds additional control to the total affect of the plasma charge on the fluid handling process.

The same surface effect of the plasma charge on the surfaces of the dispensing device can be applied to the surfaces of the fluid containing device into or onto which the fluid is dispensed. The controlled charge can improve the flow of the small fluid droplets down the side wall of a tube or microplate well and will affect the shape of the fluid droplet formation at the bottom of a tube, microplate well or fluid processing surface. As volumes being transferred

decrease, the affect of the plasma charge on the surface becomes more important. On fluid processing surfaces (surfaces onto which droplets are transferred but without a side wall defining a tube or well), the shape of the droplets on the surface determines the diameter and depth of the fluid at a defined droplet volume. The charge on the surface of the plate can alter and thereby control the forces of interaction between the droplet and the plate and, as a result, control these parameters.

Plasma technology is known in the art and is presently used in connection with a wide variety of applications. The most common uses of plasma are based on technologies that rely on the generation of plasma in a low pressure environment.

To sterilize medical devices, a technique known as glow discharge is often used, in which the items are sterilized in air, as opposed to a gas-filled evacuated chamber. For example, U.S. Patent No. 5,633,424 relates to a method of sterilizing items using water vapor-based plasma. The items to be sterilized are placed in a chamber, which is then evacuated. Water vapor is introduced into the chamber and is allowed to uniformly disperse throughout the chamber.

Electromagnetic radiation energy is then applied to the chamber, fractionating the water molecules into reactive radicals. These radicals then combine with the microorganisms on the items, effectively vaporizing the microorganisms. The by-product gases are exhausted from the chamber, and the now-sterilized items can be removed from the chamber.

U.S. Patent No. 5,700,327 recites a method for removing organic compounds from hollow containers, thereby cleaning the containers. The container is placed into a vacuum chamber, and an oxidizing gas is introduced into the chamber. An electric field is then applied to the chamber, converting the oxidizing gas into low temperature plasma, which then oxidizes substantially all of the organic compounds within the container.

U.S. Patent No. 6,059,935 discloses two methods and corresponding electrode designs for the generation of a plasma, for example, at or about one atmosphere. Using the disclosed methods, various webs, films and three-dimensional objects are beneficially treated in a reduced amount of time. A first method utilizes a repetitive, asymmetric voltage pulse to generate a plasma discharge between two electrodes. An asymmetric voltage pulse is used to generate a discharge in which a substrate can be exposed predominately to either positive or negative plasma species depending on the voltage polarity used. A second method uses the gap capacitance of an electrode pair and an external inductor in shunt to form a resonant LC circuit. The circuit is driven by a high power radio frequency source operating at 1 to 30 MHz to generate a uniform discharge between the electrode pair. Both methods have temperature controlled discharge surfaces with supply gas temperature, humidity and flow rate control. The gas flow is typically sufficient to cause a turbulent flow field in the discharge region where materials are treated. Electrode pairs implement these methods and include a metal faced electrode and a dielectric covered electrode, one or both of which have a series of holes extending through the

electrode face for supply gas flow. The second of the above-described methods will also operate with paired, metal faced electrodes, but under more restricted operating conditions.

U.S. Patent No. 6,132,813 discloses a method for modifying a substrate surface, including the step of applying a high density plasma to the substrate surface in the presence of a hydrofluorocarbon gas and a carrier gas to form an antiwetting layer on the substrate surface. Optionally, the method includes a cleaning step of contacting the slider surface with a carrier gas for a period of time effective to clean the surface.

U.S. Patent No. 6,105,589 is directed to an improved method and apparatus are provided for cleaning the specimen and interior specimen chamber of electron microscopes, and similar electron beam instruments. The apparatus consists of a glow-discharge, oxygen-radical generator placed on a specimen chamber port with an excitation source to create a low-power glow-discharge plasma inside the generator. Air or other oxygen and nitrogen mixture is admitted to the generator at a pressure between 0.3 Torr and 5 Torr. The low power glow discharge is used to disassociate oxygen preferentially over nitrogen to create the oxygen radicals. The oxygen radicals then disperse by convection throughout the chamber to clean hydrocarbons from the surfaces of the chamber, stage and specimen by oxidation to CO and H<sub>2</sub>O gases.

A number of patents have been issued for plasma generation at atmospheric pressure. Current research with these basic methods has allowed the development of a number of plasma techniques formerly only done at low

pressure to be performed at atmospheric pressure. Atmospheric plasma generation has its own set of technical advantages and disadvantages.

U.S. Patent No. 5,977,715 discloses an atmospheric pressure glow discharge plasma source without the use of an arc. The plasma chamber is capable of producing stable plasma in Ar, He and O<sub>2</sub> mixtures using a low voltage RF power supply.

U.S. Patents Nos. 5,872,426 and 6,005,349 (a division of application Ser. No. 08/820,013, filed Mar. 18, 1997, now US Patent No. 5,872,426) and 6,147,452 (a continuation-in-part application Ser. No. 08/820,013, filed Mar. 18, 1997, now US Patent No. 5,872,426) disclose a number of methods and apparatus for stabilizing glow plasma discharges by suppressing the transition from glow-to-arc by including a perforated dielectric plate with characteristics detailed in the patent. The patents detail embodiments with a wide range of electric fields including DC and RF fields of varying strength and an AC glow discharge device in which the frequency of the AC source is adjusted to be matched to the characteristics of the apertured dielectric. In this embodiment jets come out of the apertures at the proper frequency.

In US Patent No. 6,262,523 the patent discloses the device to generate a large area atmospheric-pressure plasma jet that can be operated near room temperature. The jet can extend up to 8 inches beyond the open end of the electrodes.

#### Brief Description of the Figures

Figure 1 is a diagram of the present invention.

### Detailed Description of the Invention

Figure 1 outlines the steps of the method of the present invention. First, a probe or other type of fluid handling device, preferably coated with a material optimized to the fluid characteristics of the application, such as TEFLON-coated but applying to probes with any coating, is placed into either a plasma chamber and the chamber is sealed or is placed in proximity to a low temperature, atmospheric plasma source within the area that plasma will be generated.

In the instance of using a plasma chamber, a vacuum is created in the sealed plasma chamber, and oxygen gas, along with an argon carrier gas, is introduced into the chamber and dissipates throughout the chamber. Sufficient electromagnetic energy is added to the chamber to ionize the oxygen gas within the carrier gas mixture, creating mainly O ions, free electrons, and free radicals. Because the probe has very little organic material on the surfaces when it is placed in the plasma chamber, what organic material that is present is quickly removed and the ions and free radicals have no other substance to attach to, and cling to the probe, thereby imparting a charge to the probe. The vacuum chamber is then vented, returning it to atmospheric pressure, and the now-charged probe is removed from the chamber.

In the instance of using a low temperature, atmospheric plasma, the method is similar except no vacuum or chamber is required and venting is

unnecessary. In either instance, the probe is charged by the plasma in a controlled and precise manner.

This method is performed by a machine that does not require human contact with the probe, which could dissipate the charge and possibly "contaminate" the probe. Under these conditions, the method is performed similar to a "tip wash" as is commonly performed. This method can be used as a replacement for a "tip wash", as any organic material on the probe will be ionized, oxidized and/or vaporized by the plasma as the probe is charged by the plasma.

After the probe has been plasma-charged according to the method, it can be used to pipette liquid compounds. The compounds being pipetted with the probe can be quite variable in consistency and physical properties. The major variables affecting the consistency of a liquid compound transfer are surface charge characteristics (hydrophilic to hydrophobic), viscosity, polarity (the electric charge of the solvent and solute), pH, ionic strength, and vapor pressure.

By using the plasma-charging method, the surface characteristics of a probe can be modified to optimize pipetting characteristics of different types of compounds used and otherwise reduce the interaction of the fluid and surface material. The surface characteristics can be "tuned" to the optimum requirements for a compound. By modifying the surface characteristics this manner, the pipetting system can work more optimally over a broader range of compounds and solvents, such as those used in drug discovery and other life

science applications. This control is critical when working with small volumes. At low volumes, most noticeably at single digit microliter quantities or less, compound characteristics will cause a liquid to cling to the surface it is attached to and remain attached to the column of fluid from which it is being metered, thus making the accurate and reproducible metering of these small volumes difficult. Applying a charge to the probe can overcome a liquid's tendency to cling to other surfaces and reduce a number of other phenomena that degrade the precision and accuracy of the fluid handling process.

It will be understood that the embodiment described herein is merely exemplary and that a person skilled in the art may make many variations and modifications without departing from the spirit and scope of the present invention. For example, the method can also be applied to charging a probe for use in connection with solid (i.e., dry) compounds. All such variations and modifications are intended to be included within the scope of the invention as defined in the appended claims.